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January 9, 2001

The Honorable Carol Browner
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on HPV Test Plan and Robust Summaries for Petroleum Gases

Dear Administrator Browner:

The following comments on the American Petroleum Institute's (API's) test plan for petroleum gases are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, The Humane Society of the United States, The Doris Day Animal League, and Earth Island Institute. These animal protection and environmental organizations have a combined membership of more than nine million Americans.

This test plan epitomizes the flaws and failures of the HPV chemical-testing program. It is a poorly thought-out plan that calls for unnecessary and uninformative tests on chemicals whose behaviors are already well-understood. It is an exercise in testing for testing's sake, with no concern for the impact and cost of the tests. Illustrative of the benign chemical nature of these compounds is the fact that propane, n-butane, and isobutane are all classified as Generally Recognized as Safe (GRAS) compounds by the Food and Drug Administration (FDA).[1] Unfortunately, the API fails to recognize this simple fact and does not cite any data used to make this GRAS determination. The failure to recognize and use the GRAS data specifically violates the EPA's October 14, 1999, letter to HPV participants, which specifies certain practices and principles to reduce the number of animals to be killed in the HPV program.[2] Those principles were recently reiterated in the EPA's October 31, 2000, letter to participants.[3]

This test plan calls for senseless, excessive tests on animals and offers nothing to the advancement of public health. By the API's own admission, extensive human and animal data already indicate that these compounds are relatively non-toxic, and that people are generally exposed to very low doses. There is absolutely no need to repeat these tests, yet again, on animals. In fact, the toxicity of these compounds is so low that the American Gas Association specifically requested that these compounds be exempt from the HPV program in a recent letter.[4]

Moreover, when testifying about the HPV program before the U.S. House Science Subcommittee on Energy and the Environment in June 1999, Dr. Bill Sanders, director of the EPA's Office of Pollution, Prevention, and Toxics, was questioned by Congressman Calvert about the unnecessary testing of chemicals that pose little real world risk. Dr. Sanders testified specifically that the EPA was "not requiring testing on butane."[5] We therefore intend to ask the Subcommittee to look into this proposed testing.

This test plan undermines the fundamental basis for developing chemical categories, as the API proposes to test for multiple endpoints nearly all the chemicals that make up the many substances covered in the category. This set of compounds provides a clear opportunity to apply structure activity relationships to evaluate chemical toxicity. The compounds evaluated here are simple organic compounds with a simple progression of structures and identical functional groups throughout, meeting all criteria for application of structure activity relationships as outlined in EPA guidance. If there ever was a situation in which structure activity relationships were applicable to evaluate compounds' toxicity, this set of compounds provides the simplest, most straightforward opportunity. Yet, the API has chosen to waste the opportunity to make use of existing data that would reduce both animal suffering and overall cost.

Our main objections to this test plan are as follows:

1. Existing data sufficiently describe potential hazards to both animals and humans. A thoughtful, comprehensive analysis indicates that much toxicological and exposure data on these chemicals already exist. These chemicals are accepted to be practically non-toxic in both humans and other animals. In fact, these compounds are so non-toxic that the FDA has labeled propane, n-butane, and isobutane "Generally Recognized as Safe" (GRAS). The API failed to acknowledge that these chemicals are GRAS and ignored the available data, explicitly violating the terms of the EPA's October 14, 1999, letter to HPV participants.

   Although much information exists, the API failed to report many toxicological, occupational, and environmental peer-reviewed studies. As we have repeatedly pointed out in comments on previous test plans, industries commonly ignore readily available toxicity information on these compounds. We request, yet again, that the EPA inform us how the agency intends to minimize unnecessary testing that results from incomplete data presentation.

   The available data also indicate that environmental and occupational exposures occur at very low levels—orders of magnitude less than the concentrations used in both past and proposed toxicity studies. This fact underscores a major flaw in the underlying assumption of the HPV program: High volume production does not necessarily translate to high volume exposure. With the petroleum gases, the existing literature provides detailed information demonstrating that occupational and environmental exposures are generally very low. The API has ignored existing human exposure data.

2. The test plan submitted by the API makes only minimal use of chemical categories. The API proposes to subject animals to acute inhalation, repeated dose, *in vivo* genotoxicity, and reproductive/developmental tests on *all* chemicals addressed in the plan with the sole exception of methane. This wholesale, indiscriminate testing undermines the fundamental reason for category formation: the reduction of unnecessary tests. The application of extensive testing is even more troublesome, as animal protection organizations were assured that no acute toxicity tests would be performed when chemical categories were used, due to the "data-rich" nature of the chemicals in these categories.

3. This massive test plan ignores animal welfare concerns in other ways. For example, the API proposes *in vivo* genotoxicity tests on *all* chemicals addressed in the test plan (except methane) even though *in vitro* tests exist, have already been conducted, and are presented in the robust summaries. This constitutes another clear violation of the October 1999 agreement. In addition, the API proposes to conduct a developmental toxicity test with Liquified Petroleum Gas (LPG) in addition to a reproductive/developmental test, despite the fact that the combination screening test (OECD 421) is adequate under the HPV program and reduces the numbers of animals used.

4. The test protocol does not apply "thoughtful toxicology." The API proposes to conduct toxicity tests at concentrations up to 80 times lower than accepted LC50s, the toxic doses that have been shown to kill 50 percent of animals in the studies.

The API should employ a more thoughtful approach to understanding the systematic toxicity of the alkane compounds in the group. It is clear that toxicity generally increases in these compounds with increasing molecular weight. Therefore, by comparing the toxicity of these chemicals to other higher molecular weight alkanes being evaluated in other categories—specifically the gasoline group to be submitted by the API later this year—a greater level of understanding of the hazard posed by these gases can be reached without conducting further testing.[6]

This API test plan specifically violates the following key items of the EPA's October 14, 1999, letter to HPV participants:

> "1. In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach.
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> 2. Participants shall maximize the use of existing and scientifically adequate data.
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> 3. Participants shall maximize the use of existing and scientifically appropriate categories of related chemicals and structure activity relationships.
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> 5. Participants are encouraged to use *in vitro* genetic toxicity testing to generate any needed genetic toxicity screening data, unless known chemical properties preclude its use.
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> 8. In analyzing the adequacy of screening data for chemicals that are substances Generally Recognized as Safe (GRAS) for a particular use by the Food and Drug Administration (FDA), participants should consider all relevant and available information….Participants reviewing the adequacy of existing data for these chemicals should specifically consider whether the information available makes it unnecessary to proceed with further testing involving animals. As with all chemicals, before generating new information, participants should further consider whether any additional information would be useful or relevant."

For the October 1999 agreement to have any meaning, the EPA must require that the API perform a more thoughtful review of existing data, expand the development of categories and structure activity relationships, and specifically explain why any additional testing is necessary for these compounds.

I can be reached via telephone at 202-686-2210, ext. 302, or via e-mail at <ncardello@pcrm.org>. Correspondence should be sent to my attention at the following address: PCRM, 5100 Wisconsin Ave., Suite 404, Washington, DC 20016. I look forward to your response on this important issue.

Sincerely,

Nicole Cardello, MHS
Research Coordinator

Attachment: Specific Comments

cc: The Honorable Robert C. Smith
The Honorable F. James Sensenbrenner, Jr.
The Honorable Ken Calvert
The Honorable Jerry Costello
Council on Environmental Quality